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Department of Internal Medicine

January 29, 2002

TO: Food and Drug Administration

RE: Proposed Data Safety Monitoring Committee Guidelines

DATE: January 29, 2002

Dear Sir or Madam:

I am Chair of the Data Safety Monitoring Committee of the International Breast Cancer Study Group (IBCSG), a major international group whose purpose is to perform clinical trials in early stage breast cancer. This group encompasses members from around the world, and is in part funded by the National Institutes of Health of the United States. As such, we have developed a comprehensive set of policies and standard operating procedures for the DSMC which are absolutely in line with the guidelines set forward by the National Institutes of Health [http://grants.nih.gov/grants/oprr/oprr.html, http://deainfo.nci.nih.gov/grantspolicies/datasafety.html, http://grants.nih.gov/grants/guide/notice-files/not99-107.html, http://grants.nih.gov/grants/guide/notice-files/not-OD-00.038.html, http://grants.nih.gov/grants/guide/notice-files/not98-084.html].

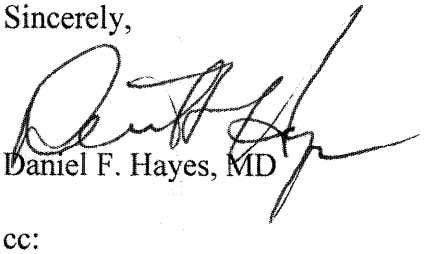
I am concerned about the recent initiative by the Food and Drug Administration to establish a second set of guidelines for DSMCs . I believe Sections 1-5 are very similar to those established by the NIH, and therefore are redundant to those of the NIH. However, I am particularly concerned about Sections 6 and 7. I feel these guidelines have completely failed to understand the distinction between pharmaceutical sponsored trials and those trials of cooperative groups sponsored by the federal government. All of these are combined under the designation of "sponsor." If these guidelines are implemented, it is possible that a trial performed by a cooperative group that will ultimately be used for FDA purposes would have to have a DSMC that is completely independent from the group sponsor (which is the NIH). Please note that all DSMCs within the cooperative groups are already independent of the pharmaceutical sponsors, and are overseen by the National Institutes of Health. While I agree that a trial that is completely sponsored and performed by a pharmaceutical company should probably have an independent DSMC, it is impractical and frankly unsafe for such a system to be established for the cooperative groups. For example, it would require the group statisticians not be part of the DSMC. At least in the meetings for the IBCSG, it is

essential that we have the study statisticians present for a clear presentation of the data and for clarification of issues as they arise during the discussions. This new policy appears to shift the responsibility for all the review of toxicity data and reporting to the DSMC. Frankly, this is impractical and, again, dangerous, since the DSMC does not have the resources or time to perform such a function. This function is already quite well done by the cooperative groups themselves.

In summary, I hope that the FDA would consider harmonizing their guidelines with those of the National Institute of Health, or even better, excluding those studies performed by the cooperative groups from these guidelines, even if these studies are designed to ultimately permit an associated pharmaceutical company to bring a drug for registration.

Thank you for considering my comments.

Sincerely,



Daniel F. Hayes, MD

cc:
Dr. Richard Gelber